The importance of the determination of the myocardial area at risk in the evaluation of the outcome of acute myocardial infarction in patients

ANDREW J. FEIRING, M.D., MARYL R. JOHNSON, M.D., JOHN M. KIOSCHOS, M.D., PETER T. KIRCHNER, M.D., MELVIN L. MARCUS, M.D., AND CARL W. WHITE, M.D.

ABSTRACT On the basis of animal studies, we postulated that the size of the perfusion field (risk area) of an occluded coronary artery would be an important determinant of outcome in patients with acute myocardial infarction. To test this hypothesis, we measured size of the risk area in 27 patients with acute myocardial infarction by the intracoronary injection of $^{99m}$Tc-macroaggregated albumin and gated nuclear imaging. After injection of the albumin spheres (5.3 ± 1.4 hr after the onset of chest pain) streptokinase was administered and in 16 of 27 patients (59%) effective thrombolysis was achieved. Since none of the patients had evidence of a prior acute myocardial infarction, the 3 day nuclear left ventricular ejection fraction (LVEF) was considered an index of infarct size. Response to thrombolysis was analyzed according to success or failure of reperfusion and the size of the risk area (small risk area less than 25%, large risk area greater than 25% of left ventricular surface area). Standard clinical indexes correlated poorly with size of the risk area: electrocardiographic variables ($r = .37$), left ventricular end-diastolic pressure ($r = .23$), cardiac index ($r = .55$), and the LVEF obtained from a right anterior oblique contrast ventriculogram ($r = .31$). The coronary vessel responsible for the acute myocardial infarction significantly influenced size of the risk area (left anterior descending, 38 ± 5% [mean ± SD] vs circumflex or right coronary artery, 17 ± 4%). However, knowledge of the site of coronary occlusion within a vessel was not helpful in predicting the size of the area at risk. For example, sizes of risk areas in patients with proximal and mid left anterior descending coronary occlusions were similar (38 ± 8% vs 33 ± 14%). When the 3 day LVEF response was analyzed as a function of risk area subset, patients with large risk areas had significantly lower LVEFs than those with small risk areas (33 ± 9% vs 56 ± 50%, $p < .01$). A strong inverse linear relationship was demonstrated between the 3 day LVEF and size of the risk area in those patients with persistent coronary occlusion ($r = .91, y = -1.19x + 75$). All cardiogenic deaths occurred in patients with risk areas greater than 33% of the left ventricular area ($p < .001$ vs small risk area). In conclusion, these studies demonstrate that accurately measured risk area size is a major prognosticator of outcome in those patients with acute myocardial infarction in whom reperfusion fails or occurs relatively late. These findings underscore the importance of the determination of risk area in patients in whom the efficacy of infarct-limiting agents is being assessed.


MANY ANIMAL STUDIES$^{1-7}$ have demonstrated that the area at risk (perfusion field deficit) subserved by the occluded coronary artery is a major independent variable that dictates ultimate infarct size. Additionally, it has been shown that knowledge of the anatomic site of occlusion of the coronary artery cannot be used to predict the size of the risk area.$^{3-6}$ In animals it was observed that if the risk area (as defined by barium angiography) was less than 18% to 20% of the left ventricular mass, no infarction occurred.$^6$ If the risk area was greater than 20% there was a close linear relationship between the size of the risk area and ultimate infarct size.$^1-7$ Experimental interventions can shift both the slope and intercept of this infarct/risk relationship in both unfavorable and favorable directions.$^7-9$ Most approaches to assessing risk area require excision of the heart.$^5, 10-12$ Lee et al.$^5$ using postmortem autoradiography, demonstrated that there was a
linear relationship between risk area and subsequent infarct size in patients who suffered fatal infarctions. Although size of the risk area has been demonstrated to be an important variable that determines infarct size, efforts to determine risk area in patients with acute myocardial infarction have been hampered by lack of a suitable method.

We have recently developed and validated in animals an accurate and reproducible experimental method for determining the in vivo, premortem risk area by use of intracoronary administration of \(^{99}\)Tc-macroaggregated albumin (TcMAA) in conjunction with gated nuclear imaging.\(^3\) We have introduced this technique into the cardiac catheterization laboratory where risk area was determined in patients with acute myocardial infarction before they received thrombolytic therapy with intracoronary streptokinase.

The purpose of this study was to extend the concept to humans that size of the risk area, determined in vivo, is a key determinant of the outcome of acute myocardial infarction. In addition, we examined specific factors that might influence this variable, such as the coronary artery involved and the site of occlusion within a given coronary vessel. We also assessed the ability of several commonly available clinical indexes to predict size of the risk area.

Methods

**Patient selection.** The study group consisted of 27 patients who were admitted for intracoronary thrombolytic therapy of acute myocardial infarction at the University of Iowa Medical center between July 1983 and November 1984. Criteria for admission to this study were as follows:

1. History of prolonged chest pain (greater than 30 min) and symptoms consistent with acute myocardial infarction.
2. Onset of chest pain less than 8 hr preceding arrival at the cardiac catheterization laboratory.
3. Age less than 80 years.
4. Electrocardiographic (ECG) changes suggestive of transmural myocardial infarction, defined as at least 2 mm ST segment elevation above the J point in at least two leads.
5. Persistent ST segment elevation after administration of sublingual nitroglycerin (0.4 mg) and sublingual nifedipine (10 mg).
6. No history or ECG evidence of prior myocardial infarction.
7. No history of prior coronary artery bypass graft surgery, congenital or valvular heart disease, or other known cardiovascular diseases.
8. No recognized contraindication to the administration of streptokinase.
9. Total proximal or midvessel occlusion of the infarct-related artery that persisted despite sublingual nifedipine and intracoronary nitroglycerin.
10. No patients were excluded because of hemodynamic instability.
11. Radionuclide left ventricular ejection fraction (LVEF) determinations were obtained on the third day (72 hr) after cardiac catheterization. Only data from those patients who had a 3 day LVEF determination were included in the statistical analysis.

All patients gave informed written consent. The study protocol was approved by the Human Subjects Research Committee of the University of Iowa.

A total of 47 patients were considered for enrollment. One patient declined to participate. At the time of catheterization nine patients (19%) were found to have subtotal coronary artery occlusion and consequently were not injected with the total dose of TcMAA. Three patients (6%) were excluded because of evidence of previous myocardial infarction. Three patients (6%) died before acquisition of the 3 day LVEF (two patients of cardiogenic shock, one patient with splenic rupture) and thus their data were excluded from statistical analysis. Six patients (13%) were excluded because of technically inadequate studies. Thus 27 patients studied in a consecutive manner constituted the final study group.

**Protocol.** In the emergency room all patients received standard therapy for acute myocardial infarction, which included intravenous lidocaine (75 to 100 mg intravenous bolus followed by a 2 mg/min drip), oxygen via a nasal cannula (4 l/min), and morphine sulfate intravenously as needed to control pain. Before catheterization, patients who were hemodynamically stable were premedicated with 50 mg iv diphenhydramine and 25 mg subcutaneous promethazine.

**Catheterization protocol.** By the Seldinger femoral-arterial and venous approach, the following steps were sequentially performed after administration of a 5000 unit bolus of intravenous heparin. Initial assessment of right and left heart pressures was followed by left ventricular cineangiography in the 40 degree right anterior oblique projection. Selective coronary angiography was performed in multiple projections. After angiographic evaluation, 400 μg of intracoronary nitroglycerin was delivered into the infarct-related artery that remained totally occluded. If the artery remained completely occluded, then 10 mCi of TcMAA was delivered in divided doses into the left main and right coronary ostia via selective coronary catheters. After administration of the TcMAA, an intracoronary bolus of 20,000 units of streptokinase was administered into the infarct-related artery, followed by an infusion of intracoronary streptokinase at 4000 units/min. Every 15 min thereafter if reperfusion failed to occur an additional bolus of 20,000 units was administered and the intracoronary infusion was continued. If reperfusion was unsuccessful this sequence was continued for a total of 1½ hr (480,000 units). If the artery reperfused, streptokinase was administered for an additional 30 min after angiographic evidence of vessel patency. All patients remained systemically heparinized for 10 days after cardiac catheterization and an activated partial thromboplastin time of 2 to 2½ times normal was maintained.

**Risk area protocol: administration of TcMAA.** A total of 10 mCi of intracoronary TcMAA (200,000 particles) was administered to each patient. Quality control of the macroaggregates was assured by assessment of the injectate for particle size, number, and labeling efficiency. Before the intracoronary injection of TcMAA, the angiographic catheter was optimally positioned to avoid selective injection or noticeable contrast streaming. After the final contrast injection, 1 min was allowed to elapse before the injection of the radiolabeled particles to minimize any potential effect of contrast-induced coronary vasodilatation on particle distribution. Thereafter the residual contrast was aspirated from the coronary catheter and the TcMAA was slowly infused into the coronary artery over a period of 15 to 30 sec. We administered 8
mCi of TcMAA into the left coronary artery and 2 mCi of TcMAA into the right coronary. The catheter was then flushed of residual radioactivity with a slow injection of 10 ml of normal saline. Pulmonary capillary wedge pressure, arterial blood pressure, and the electrocardiogram were continuously monitored before and for 2 min after injection of the TcMAA.

Imaging of the risk area. Gated images were obtained in two projections with the use of a Searle low-energy small-field-of-view camera (Siemens, LEM) interfaced with a Medical Data System (MDS-A') computer. The camera's energy analyzers were set at 140 keV with a 15% window. A low-energy, all-purpose, parallel-hole collimator was used. Twelve gated images per cardiac cycle were acquired in a 64 × 65 matrix with the use of byte mode data recording at 1.5 to 2 magnification. Each of the twelve gated images contained 200,000 counts per frame. Imaging time per projection ranged between 2 and 5 min. Administration of the TcMAA did not significantly delay institution of streptokinase therapy, because gated imaging was performed during continuous administration of the intracoronary infusion of streptokinase. Images were obtained in the left anterior oblique (LAO) and right anterior oblique (RAO) projections. For images acquired in the left anterior oblique projection (30 to 45 degrees LAO), the camera face was positioned to obtain maximal separation of the right and left ventricles as well as optimal visualization of the septum. In this projection the right ventricular free wall was also well visualized. In the right anterior oblique projection the camera was positioned to obtain the greatest surface area of the ventricle.

Assessment of coronary angiograms. Coronary arteriograms were analyzed by two observers. A vessel was said to be significantly diseased if the luminal diameter was reduced by more than 50%. The site of coronary artery occlusion was graded as either proximal or mid vessel, according to the American Heart Association classification.14 For the right coronary artery, proximal occlusions were defined as occurring between the coronary ostium and the first right ventricular branch and mid vessel occlusions as between the first right ventricular branch and the acute marginal artery. For the left anterior descending artery occlusions were proximal if they occurred between the left main ostium and the first septal perforator and mid vessel if they were between the first septal and second diagonal branch. Collateral vessels were said to be present if any segment of the infarct-related artery distal to the occlusion filled in a retrograde fashion.

Analysis and assessment of LVEF. LVEF was assessed by radionuclide ventriculography on the third hospital day for each surviving patient. Gated resting ventriculograms were obtained by labeling of red cells in vivo with 25 mCi of 99mTc.15 The left ventricular ejection fraction was calculated from the 45 degree LAO image. The accuracy and precision of these methods have been described elsewhere.16,17

Analysis of risk area. The technique for analyzing the area at risk in vivo has been previously described.13 Briefly, for patients with either left anterior descending or circumflex coronary artery occlusion the LAO view was used to assess the risk area: for patients with right coronary artery occlusion the RAO view was analyzed. The end-diastolic frame of each of these studies was isolated and the ventricular perimeter was traced with the light pen. In the LAO projection the ventricular cavity and the hypoperfused zone were delineated. For RAO projections, only the epicardial boundaries and the hypoperfused zone were defined. The left ventricular risk area was calculated as the planimetric ratio between the area of the hypoperfused zone and the projected area of the entire left ventricular myocardium.

Patients were divided into two groups based on the size of the area at risk: patients with small risk areas, i.e., those less than 25% of left ventricular wall area, and patients with large risk areas, or those greater than 25% of the left ventricular wall area.

Relationship between the risk area and the presenting electrocardiogram, hemodynamics, and acute LVEF

Electrocardiograms. A 12-lead electrocardiogram was obtained in all patients while they were undergoing evaluation in the emergency room. The electrocardiogram was analyzed according to the following criteria: (1) sum of ST segment elevation in all involved leads, (2) presence of significant (< 0.03 mm/sec wide) q waves in the infarct-related leads, (3) sum of the leads with both ST segment elevation and q waves. Patients with left or right bundle branch block were excluded from ECG analysis (n = 2).

Hemodynamics. Hemodynamic evaluation was done before institution of thrombolytic therapy. Presenting heart rate was evaluated from the initial electrocardiogram. Arterial blood pressure was recorded in the catheterization laboratory after access to the femoral artery had been obtained. Cardiac output was determined by the thermodilution technique. The cardiac output was determined by averaging five sequential measurements of cardiac output. Cardiac index was derived by dividing the patient's cardiac output by body surface area. Left ventricular end-diastolic pressure was obtained immediately before contrast ventriculography with a fluid-filled No. 8F pigtail catheter connected to a Statham 23DHBY strain gauge and was recorded at 100 mm/sec.

Initial LVEF. Contrast ventriculography was performed through a No. 8F pigtail catheter with the use of 35 to 50 ml of meglumine sodium diatrizoate. The images were acquired in a 40 degree RAO projection. The left ventricular silhouette was planimetered in end-diastole and end-systole. Studies were excluded if the preceding cardiac cycle demonstrated a premature ventricular contraction. Ejection fraction was calculated by standard techniques.

Statistical analysis. Students t-test (paired or unpaired) was used to compare two groups with approximately normal distribution. The correlation between the risk area and 3 day radionuclide LVEF, as well as the relationships between ECG variables, cardiac index, angiographic LVEF, and heart rate and blood pressure were analyzed by the least square method of determining linear regression. The significance of the correlation coefficient value, slope, and y intercept were calculated. Nonparametric group comparisons were made when appropriate with the use of the Mann-Whitney test. Chi-square analysis was performed for data in a 2 × 2 contingency table. Significance was accepted at a level of p < .05. Data are presented as the mean ± SD.

Results

Patient characteristics. The patient data were analyzed according to the following major variables: immediate success or failure of thrombolysis (determined at the time of leaving the catheterization laboratory), size of the risk area of the infarct-related artery, number of significantly diseased vessels other than the infarct-related artery, and collateral vessels to infarct-related artery (table 1). The average age of the patients was 57 ± 11 years (mean 55.7 ± 11; women 59.9 ± 12). The average time from onset of chest pain to streptokinase infusion was 5.25 ± 1.4 hr (men 5.2 ± 1.5; women 5.2 ± 1.1). At the conclusion of streptokinase therapy a systematic fibrinolytic state was achieved in all patients, as evidenced by a persistent
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TABLE 1
Baseline angiographic and risk area findings in the patient study group

<table>
<thead>
<tr>
<th>Infarct-related artery</th>
<th>Successful reperfusion (%)</th>
<th>Risk area &lt;25% (n)</th>
<th>Risk area &gt;25% (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCA</td>
<td>10</td>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>LAD</td>
<td>13</td>
<td>62</td>
<td>2</td>
</tr>
<tr>
<td>Cx</td>
<td>4</td>
<td>50</td>
<td>4</td>
</tr>
</tbody>
</table>
| No. of Diseased vessels
  One vessel             | 11                          | 50                | 6                 |
  Two vessels            | 13                          | 62                | 7                 |
  Three vessels          | 4                           | 75                | 3                 |
| Collaterals to infarct-related artery | 8                          | 38                | 6%                |

n = number of patients; RCA = right coronary artery; LAD = left anterior descending coronary artery; Cx = circumflex coronary artery.

*Diseased vessel defined as greater than 50% narrowing of luminal diameter of a non-infarct-related artery.

*Collateral to infarct-related artery visually apparent.

*Statistically significant at p < .05. All patients in this group had right coronary artery occlusions.

depression of fibrinogen and elevation of levels of fibrin split products. Analysis of risk area, hemodynamics, and the coronary arteriogram. The mean heart rates for patients with small vs those with large risk areas were 84 ± 14 and 82 ± 14 beats/min (p = NS). Likewise, the mean arterial blood pressures for these two groups were 95 ± 11 and 91 ± 14 mm Hg (p = NS). There was no statistically significant difference in the frequency of two- or three-vessel coronary artery disease in patients with small risk areas as compared with those with large risk areas (table 1). As a group, the patients with small risk areas (< 25%) usually had either right coronary or circumflex coronary occlusions and patients with large risk areas had occlusions of the left anterior descending artery (figure 1). In patients with right coronary artery occlusions, the mean risk areas for proximal and midvessel occlusion were 20 ± 2% and 17 ± 5% (p = NS) (figure 1). For patients with left anterior descending artery occlusions, the mean risk areas for proximal and midvessel occlusions were 38 ± 8% and 33 ± 14% (p = NS) (figure 1). It should be noted that because our sample sizes were small, if a modest effect of site of occlusion on risk area size had existed, it would not have been detectable.

Size of the risk area. The range of risk areas for right and circumflex coronary artery occlusions was 10% to 25%, with a mean of 17.6 ± 4% (figure 2). The range of risk areas for the left anterior descending artery was 14% to 49% of the left ventricular surface area (mean 39 ± 5%) (figure 2). There was a statistically significant difference in size of the risk area for patients with left anterior descending occlusions and those with right and circumflex artery occlusions (p < .001), although some overlap was present (figure 1). When size of the risk area was evaluated as a function of the success or failure of coronary artery reperfusion, the size in the two groups was approximately equal (figure 3, left). When patients were grouped with regard to large and small risk areas, the number of patients in whom reperfusion was successful and in whom it was unsuccessful was similar (figure 3, right). However, when these patients were stratified according to size of the risk area, as expected a large separation was observed between the mean areas for each group (17.6% vs 39.2%, small vs large).

Relationship between the 3 day LVEF and size of the risk area. When 3 day LVEF was evaluated as a function of the success or failure of coronary artery reperfusion, no statistically significant difference was observed (figure 4, left). However, when patients were stratified on the basis of the size of the risk area rather than success or failure of reperfusion, a statistically significant difference in 3 day LVEF was noted (p < .001) (figure 4, left). Patients with large risk areas (39.4 ± 5.1%) had a significantly lower LVEF (33 ± 9%), regardless of the success or failure of reperfusion. Patients with small risk areas (17 ± 5%) had normal LVEFs (56 ± 6%), regardless of reperfusion status.

There were 11 patients with large risk areas that survived to the third hospital day. The mean LVEFs for the successful and unsuccessful reperfusion groups were not significantly different (successful 32.5 ± 10.5% vs unsuccessful 32.8 ± 6.7%). Likewise, there was no statistically significant difference in size of the
risk area between these two groups (successful 42 ± 4.6% vs unsuccessful 35.4 ± 3.4%). Fourteen patients received streptokinase within a mean elapsed time of 4.0 ± 0.5 hr. Reperfusion was significantly more successful in those patients who received streptokinase in under 5 hr (10 of 14 vs five of 12 of those who received streptokinase later, p < .001). There was no difference between early and late reperfusion groups with regard to size of the risk area (27 ± 14 vs 25 ± 10) or 3 day ejection fraction (46 ± 14% vs 47 ± 14%).

**Evaluation of standard clinical variables vs scintigraphic risk area.** In this study ECG variables, presenting hemodynamics, and initial contrast LVED were compared to size of the risk area as determined by the intracoronary injection of TcMAA and gated nuclear imaging. In general these standard clinical variable correlated poorly with size of risk area (figure 5).

**Infarct/risk relationship.** With the use of the 3 day LVEF as an indirect measure of infarct size, a strong inverse linear relationship was demonstrated between risk area and 3 day LVED in patients with unsuccessful coronary artery reperfusion (r = .91, y = 1.19x + 75) (figure 6). The relationship between risk area and 3 day ejection fraction in all patients, regardless of outcome of thrombolytic therapy, was represented by r = .77, y = 0.87x + 69 (figure 5). For patients who underwent successful thrombolysis the relationship between size of the risk area and 3 day ejection fraction was weaker (r = .69, y = 0.72x + 66). There was no statistically significant difference between the various slopes or intercepts of these regression equations.

**Mortality.** No patient died during cardiac catheterization. Five patients died from cardiogenic causes during the course of the study. All patients who died had risk areas greater than 33% regardless of reperfusion status (figure 1). Five of thirteen patients with risk areas greater than 33% died within 7 days of admission. Of these five who died, coronary artery reperfusion was successful in two and failed in three. Four of five patients had proximal occlusions of the left anterior descending artery. The mean risk area of the patients who died was greater (41 ± 3%) than the risk

![FIGURE 2](image-url) **FIGURE 2.** Relationship between site of coronary artery occlusion and size of the risk area.

![FIGURE 3](image-url) **FIGURE 3.** Left, When patients are evaluated according to success or failure of reperfusion the mean risk areas in the two groups are not significantly different. Right, As expected there is a large difference between those patients with large and small risk areas.

![FIGURE 4](image-url) **FIGURE 4.** Left, When patients are evaluated according to success or failure of reperfusion, no difference is noted in the therapeutic response (3 day LVEF). Right, When patients are evaluated according to size of the risk area the therapeutic response (LVEF) is significantly dependent on this variable.
area of the surviving patients (24 ± 12%, p < .005).

Postmortem examinations were obtained in the two patients who died of cardiogenic shock within 24 hr of myocardial infarction and the determination of risk area. Based on the residual TcMAA radioactivity that remained in the myocardium, postmortem autoradiography in these patients demonstrated left ventricular risk areas of 43% and 46%, respectively. The gated and diastolic risk area obtained at the time of catheterization in these same patients was 42% and 43%, respectively.

Long-term follow-up. The average duration of follow-up in the 24 surviving patients was 14.7 ± 4.9 months (range 6.5 to 23 months). All patients who survived the fourth hospital day (85%) were alive at follow-up. No patient with right coronary artery occlusion died because of cardiac dysfunction.

Discussion

There are three salient findings of this study:

1. In patients who present with acute myocardial infarction, similar sites of occlusion within a single coronary artery result in a wide range of risk areas. A priori knowledge of the location of coronary artery occlusion within a given vessel (proximal vs mid) could not accurately predict subsequent size of the risk area.

2. Standard clinical indexes (ECG variables, left ventricular end-diastolic pressure, cardiac index, and monoplanar angiographic LVEF) provide inaccurate estimates of the size of the risk area.

3. The size of the risk area is a dominant predictor of outcome in patients experiencing their first myocardial infarction.

FIGURE 5. Relationship between size of the risk area and various standard clinical variables. A. Sum (Σ) of ST segment elevation in all leads vs size of the risk area. B. Acute angiographic LVEF vs size of the risk area. C. Left ventricular end-diastolic pressure (LVEDP) versus size of the risk area. D. Cardiac index vs size of the risk area.

FIGURE 6. Infarct/risk relationship for the entire study group (solid line) and for those in whom coronary artery reperfusion was unsuccessful (broken line). The unsuccessful reperfusion group demonstrates a strong inverse linear relationship between size of the risk area and 3 day LVEF.
dial infarction if the risk area is small, if thrombolysis is unsuccessful, or if it occurs relatively late (greater than 5 hr after the onset of chest pain). In patients with unsuccessful thrombolysis the 3 day LVEF is significantly and linearly correlated with the size of the risk area. Patients with small risk areas have very low mortality and well preserved left ventricular function regardless of success or failure of reperfusion, whereas patients with large risk areas are at risk for significant mortality and marked deterioration of left ventricular function.

**Rationale for use of 3-day ejection fraction as an indirect measure of infarct size.** Since there is no reliable direct measure of infarct size applicable to patients, we used the 3 day radionuclide LVEF as an index of the functional integrity of the myocardium. In the absence of any previous myocardial dysfunction, the integrity of the recently infarcted left ventricle should be related to the loss of functional myocardium and thus may be indirectly measured by the change in global LVEF. A recent animal study by Schneider et al. demonstrated that the change in LVEF in dogs after proximal coronary artery occlusion was linearly related to the ultimate infarct size. A previous study from our laboratory and those by others have demonstrated that there is no significant difference between mean LVEF determinations obtained in patients with acute myocardial infarctions 72 hr and 2 weeks to 1 month after the acute event.

Nonetheless, the isotope LVEF is by no means a perfect measure of infarct size. Acute regional changes in left ventricular function can compensate for reduced contractility in the infarct-related area. Furthermore, in patients with successful early reperfusion a certain quantity of myocardium may be stunned, and thus at first might not contribute to overall left ventricular function, although with metabolic recovery left ventricular function of the impaired muscle may improve over time. Despite these problems, at this time LVEF is the best indirect measure of infarct size in a patient who has sustained no prior myocardial damage.

**Infarct/risk relationship in vivo in humans.** In this study we measured an infarct/risk ratio in vivo for each patient. If infarct/risk relationships in patients are similar to those measured in animal experiments, then we would expect that for small risk areas there should be little or no functional left ventricular impairment. Patients with large risk areas in whom reperfusion is not achieved should demonstrate profound depression of the left ventricular function. Patients with large risk areas in whom reperfusion is successful might be expected to demonstrate a heterogeneous response since the variables of time from occlusion to reperfusion, myocardial oxygen consumption, and level of residual collateral flow are still uncontrolled. The findings of this study confirm many of these hypothetical constructs. Patients with small risk areas (less than 25% of the left ventricular area) had normal 3 day LVEFs regardless of the success or failure of reperfusion. Moreover, all these patients were alive at follow-up. Patients with large risk areas and unremittant coronary artery occlusion demonstrated a profound depression of LVEF that was linearly related to risk area size (figure 5). The major determinant of functional integrity of the myocardium in this group was the size of the risk area. Patients with large risk areas who did not undergo successful reperfusion had a 3 day LVEF that demonstrated a strong inverse relationship to the size of the area. Patients with large risk areas who underwent successful reperfusion demonstrated a heterogeneous response to thrombolytic therapy. The sample size of our patients with large risk areas was not large enough and they did not undergo reperfusion early enough to demonstrate whether successful thrombolysis shifts the infarct/risk relationship in a favorable direction.

In conclusion, the results of this study extend to humans the important concept that the size of the risk area is a dominant determinant of outcome after coronary artery occlusion. Furthermore, our data suggest that many readily available indexes, such as the patient’s electrocardiogram, cardiac output, left ventricular end-diastolic pressure, the LVEF measured acutely with a RAO contrast ventriculogram, and coronary anatomy cannot be used to accurately predict size of the risk area. Thus, this study in humans suggests that quantitative measurements of risk area may be critical in studies directed toward evaluating the efficacy of clinical infarct-limiting strategies. In view of our findings, development of rapid, precise approaches to the assessment of the size of the risk area, such as tomographic imaging of intravenously administered radionuclides, should be encouraged.

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